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Original Research Article

Association of Leucocyte Count, Troponin I and Serum PRL Level in Pregnants as Predictors of Cardiomyopathy with Hypertensive Disorders

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Abstract

Introduction: Hypertension and proteinuria after the 20th week of pregnancy characterize the complex illness known as preeclampsia. Activation of leukocytes is implicated, which is thought to cause inflammation and vascular injury. Cytokines released by activated leukocytes cause damage to the endothelium. Activation of neutrophils has been explicitly linked to the increased inflammatory response observed in preeclampsia.

Aims and Objectives: The study aims to assess leukocyte count, Troponin I levels, and serum PRL levels in pregnant women with hypertensive diseases.

Methods: In a hospital setting, a prospective cohort study was carried out with the participation of 265 hypertension patients. The purpose of the study was to collect blood samples from preeclampsia and eclampsia patients in order to evaluate the levels of biomarkers. The patients were then monitored for a period of time equal to five months after delivery to ascertain whether or not they had acquired peripartum cardiomyopathy (PPCM).

Results: The main findings of the study indicate that individuals with PPCM had significantly higher mean total leucocyte counts compared to those without PPCM. The average serum prolactin levels were also significantly elevated in the PPCM group. These results suggest a potential association between higher leucocyte counts, elevated serum prolactin levels, and the presence of PPCM. Additionally, the study found that Troponin I levels differed significantly between the two groups, indicating its potential as a biomarker for distinguishing individuals with PPCM.

Conclusion: The study has concluded that the outcomes of this study indicate that markers such as the total leucocyte count, serum prolactin, and Troponin I can be considered early predictors of PPCM.

Keywords: Prolactin, Troponin, Peripartum, Cardiomyopathy.

Introduction

Whenever acute cardiovascular (CV) disease is suspected in the general population, cardiac biomarkers are often employed; however, the behavior of these biomarkers during pregnancy seems less well understood. The symptoms of heart

dysfunction are frequently mimicked in pregnant people, and pregnancy problems might include CV illness. The maternal heart has greater hemodynamic demands during pregnancy [1]. The cardiovascular system is altered due to significant neurohormonal changes, enabling adaptation to the higher demands of a typical pregnancy. It might be challenging to differentiate between typical pregnancy-related symptoms of lower extremity fatigue, dyspnea, decreased exercise tolerance, and tiredness edema in pregnant people from those with heart failure.

Additionally, cardiovascular symptoms like cardiomyopathy might be pregnancy problems. Cardiac biomarker testing in pregnancy is less well-known than its application for identifying and following up on individuals with suspected or confirmed cardiovascular disease [2]. Consequently, a greater comprehension of whether and how cardiac biomarkers may be used in clinical practice is crucial to pinpointing pregnant women requiring further cardiovascular testing. During this lecture, we recommend how to utilize these instruments most effectively in clinical practice according to the available data and summarise our current understanding of the application of cardiac biomarkers during pregnancy [3].

Proteinuria and gestational hypertension after the 20th week of pregnancy are the two symptoms that characterize the severe pregnancy complication known as preeclampsia (PE). Hypertension is defined as blood pressure that is more than 160/110 mmHg for severe manifestations of PE and 140/90 mmHg in moderate PE [4]. Depending on the problem is severity, proteinuria is defined as having over 0.3 to 5 g of protein per gram of urine throughout the day. Neonates with Low birth weights based on their gestational ages are considered small-for-gestational-age (SGA) and are linked to PE in roughly one out of every five occurrences. Three to five percent of all pregnancies worldwide are said to have PE. Redman, Horrobin, and others originally proposed a function for PRL in preeclampsia about 1975; however, at the time, they did not take into account the potential involvement of antiangiogenic PRL-fragments because these were only shown to have vascular effects much later in 1991 [5]. Since then, growth hormone (GH), placental lactogen (PL), and PRL's antiangiogenic fragments, which share certain structural traits, biological effects, & signaling pathways, have risen to the vasoinhibin family., and other molecules. Numerous endocrine, paracrine, and autocrine actions are produced by vasoinhibin [6]. It is made when the bones cut the long loop linking the third and fourth alpha helices of PRL morphogenic protein 1 (BMP-1), cathepsin-D, and matrix metalloproteinases (MMP). One of its primary target tissues is the vascular system, and its side effects additionally involve the suppression of angiogenesis, vasodilation, and permeability. In a normal pregnancy, the concentrations for each of the vasoinhibin precursor molecules-PRL, GH, & hPL-significantly alter in the blood. In PE, compared to a typical pregnancy, the levels of circulating hormones shift, as do the activity and amount of the protein-cleaving enzymes that control the production [7].

When utilizing radioimmunoassays upon post-mortem cardiac tissue, the first commonly used techniques for detecting cTn, also the initial generation, were capable of detecting high TnI concentrations exceeding 10,000 ng/L, as in the case of extensive cardiac necrosis. Even fourth-generation assays, with quoted limits of detection between 2-200 ng/L, could identify circulating cTn in just a tiny percentage of healthy people [8]. Advances in technology have increased sensitivity by enhancing precision and enabling earlier detection. As a result, these outdated techniques cannot pick up on the subtle impacts of micro-necrosis.

Since the advent of new fifth-generation cTn assays, which are up to 1000 times more accurate than their forerunners, it has been able to accurately assess concentrations as low as 0.1–5 ng/L [9].

Hypertension, a multisystem condition called preeclampsia, may develop in pregnant women. Preeclampsia's exact cause is unknown. However, several factors, including a genetic predisposition, are believed to be responsible for predisposition, aberrant placental invasion, & immunologic or excessive inflammatory responses. Research shows Leukocyte activation also plays a substantial part in preeclampsia's illness process [10]. There is significant evidence of leukocyte activation in preeclampsia-affected women, including elevated superoxide production and higher integrin CD11b & CD64 expression in monocytes and neutrophils. The cytokine interleukin-8 and the tumor necrosis factor, among others, are released by activated leukocytes and can regulate endothelial function [11]. In this pregnancy disease, it is thought that interactions among the vascular endothelium, platelets, and activated leukocytes cause vascular damage. Additionally, neutrophil activation is believed to be a significant factor in the heightened inflammatory responses within the mother's vascular system in preeclampsia [12].

Materials and Methods

Research design

This prospective cohort study in hospitals aims to identify risk factors for PPCM among pregnant women with hypertensive conditions. From November 2018 through April 2020, researchers from the Department of Obstetrics and Gynecology at B.L.D.E. This prospective study aimed to understand better the characteristics of cardiomyopathy in women who experienced hypertension during pregnancy, preeclampsia, or eclampsia. All individuals gave informed consent to participate in these studies and subsequent follow-ups. Patients were monitored for one week in the hospital to look for signs of PPCM, such as shortness of breath, pedal edema, tachycardia, and a drop in oxygen saturation (SpO_2). When these symptoms were present, a 2D ECHO was performed to be sure. Those who did not experience any cardiac symptoms during their hospital stay were released and monitored in the outpatient department at 1-, 3-, and 6-month intervals. Patients who could not keep their scheduled follow-up appointments were contacted by phone to see whether they were experiencing any symptoms that might be related to PPCM. Those who complained of symptoms were contacted to have an ECHO test. Clinical characteristics and heart health of pregnant women with hypertension disorders were evaluated and followed over time, thanks to this study's design.

Inclusion criteria

1. All patients diagnosed with hypertensive disorders of pregnancy (gestational hypertension, preeclampsia, eclampsia, i.e., antepartum and postpartum eclampsia) who is in labor, or the delivery is planned within 24 hours.
2. Gestational age > 24 weeks.
3. Patients give informed and written consent for investigations and follow-ups.

Exclusion criteria

1. Gestational Diabetes Mellitus
2. Pre-Existing Cardiac Disorders
3. Chronic Hypertensive Patients
4. Patient’s with Hemoglobin levels less than 7gm/dl.

Statistical Analysis

The study has used SPSS 25 for effective statistical analysis. The continuous data has been written in mean ± standard deviation while the discrete data has been presented as frequency and its respective percentage. The study as employed

ANOVA as the statistical tool for its analysis. The level of significance was considered to be P<0.05.

Ethical approval

The Institutional Ethics Committee of the Obstetrics and Gynecology Department at B.L.D.E. (Deemed To Be University) Shri B.M. Patil's Medical College, Hospital, and Research Centre in Vijayapura has approved this study. Ethical approval guarantees that the study will comply with accepted ethical rules and principles, protecting the participants' safety, privacy, and anonymity.

Result

When comparing the two groups, those with PPCM had a higher mean total leucocyte count (17,166.1) than those without PPCM (15,056.3). The standard deviation was 1,908.1 from the mean difference of 2,109.8. The p-value for statistical significance was not significantly different from 0.05. The average serum prolactin level in the PPCM group was 171.3, while it was only 150.6 in the control group. The standard error for the mean disparity was 15.55 standard deviations. Serum prolactin levels significantly differed between the two groups (p = 0.007) (Figure 1).

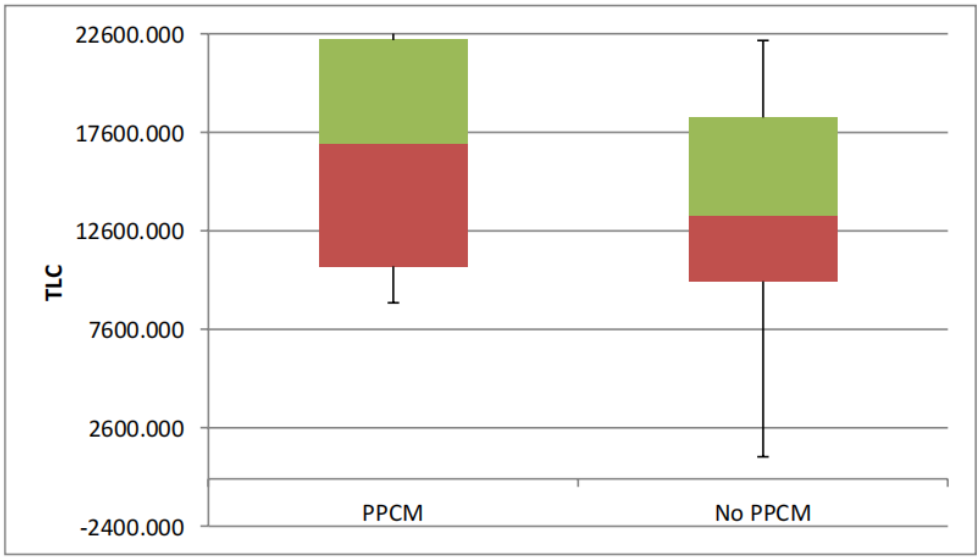

Figure 1: Comparison of leucocyte count among the study participants

Table 1 compares the leucocyte count among the study participants, specifically focusing on the total leucocyte count and serum prolactin levels in participants with peripartum cardiomyopathy (PPCM) and participants without PPCM (no PPCM). For the total leucocyte count, the table shows that the mean count for participants with PPCM (23 individuals) is 17,166.1 with a standard deviation of 9,105.3. The mean count for participants without PPCM (242 individuals) is 15,056.3, with a standard deviation of 8,711.2. The mean difference between the two groups is 2,109.8, and the standard error difference is 1,908.1. The t-value is 1.1057, with 263 degrees of freedom. The p-value is 0.05, indicating a statistically significant difference in the leucocyte count between the two groups.

Regarding serum prolactin levels, the table shows that participants with PPCM have a mean level of 171.3 with a standard deviation 72.1. On the other hand, participants without PPCM have a mean level of 129.4 with a standard deviation of 61.7. The mean difference is 41.95, and the standard error difference is 15.549. The t-value is -2.698, with 263 degrees of

freedom. The p-value is 0.007, indicating a statistically significant difference in serum prolactin levels between the two groups. The table indicates that participants with PPCM have higher total leucocyte counts and serum prolactin levels than those without PPCM. These findings suggest a potential association between these parameters and the presence of peripartum cardiomyopathy.

Table 1: Comparison of leucocyte count among the study participants

Total Leucocyte Count								
Morbidity	**N**	**Mean**	**Std. Deviation**	**Mean difference**	**Std. Error Difference**	**t-value**	**Df**	**P Value**
PPCM	23	17166.1	9105.3					
No PPCM	242	15056.3	8711.2	2109.7646	1908.1171	1.1057	263	0.05
Serum Prolactin								
PPCM	23	171.3	72.1					
No PPCM	242	129.4	61.7	41.9500	15.5490	-2.698	263	0.007

Based on the table provided, it can be observed that the average leucocyte count in patients with peripartum cardiomyopathy (PPCM) was 17,166±9,105.3, whereas, in patients without PPCM, it was 15,056±8,711.2. The difference in mean leucocyte count between the PPCM and non-PPCM groups was statistically significant, as confirmed by the Unpaired T-test.

The study found that those with PPCM had a mean Troponin I level of 0.064, whereas those without had a level of 0.04. There was an average disparity of -0.3181 and a margin of error of 0.8184. The degrees of freedom were 263, and the t-value was -0.389. A statistically significant difference in Troponin I levels was observed between the two groups (p = 0.049). Based on these results, Troponin I levels could be used as a biomarker to differentiate between those with and without PPCM (Figure 2).

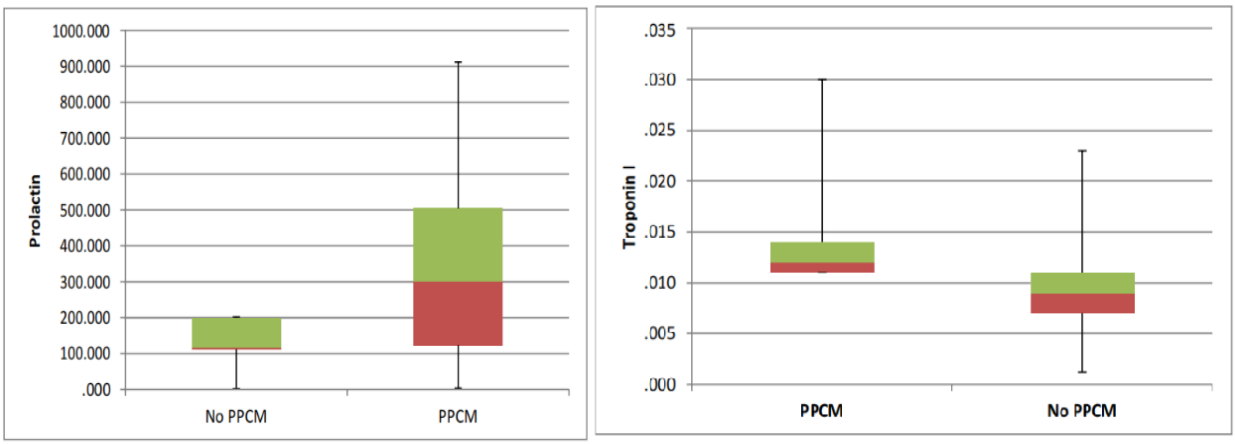

Figure 2: Comparison of serum Prolactin and Troponin I among the study participant

Table 2 compares Troponin I levels among the study participants. In the PPCM group, consisting of 23 individuals, the mean Troponin I level was 0.064 with a standard deviation of 0.233. On the other hand, in the non-PPCM group with 242 participants, the mean Troponin I level was 0.04 with a standard deviation of 3.91. The difference in mean Troponin I levels between the PPCM and non-PPCM groups was -0.3181, with a standard error of 0.8184. The t-value obtained was -0.389,

which was statistically significant, with a p-value of 0.049.

Table 2: Comparison of Troponin I among the study participants

Troponin I								
Morbidity	**N**	**Mean**	**Std. Deviation**	**Mean difference**	**Std. Error Difference**	**t-value**	**Df**	**P Value**
PPCM	23	0.064	0.233	-0.3181	0.8184	-0.389	263	0.049
No PPCM	242	0.04	3.91					

Discussion

To compare preeclampsia (PE)-affected women's platelet & white cell parameters to healthy pregnant women's. As PE progressed, WBC, ANC, MPV, PDW, P-LCR, and NLR rose. PTC dropped as the sickness got worse. The therapy of PE may be aided by assessing these measurements as a supplementary clinical sign for determining severity [13]. In both individuals. In both cases of hypertension and without it, the research aimed to look at the relationship between circulating quantities hs-cTn), a high-sensitivity cardiac troponin, during the various prenatal trimesters. Women who were pregnant or recently gave birth were included in this prospective cross-sectional study at ages 18 and 35 with no other medical conditions [14]. For hs-TnI, serum samples were examined. Most young pregnant women can have their cardiac troponin levels evaluated 2% of individuals with a high-sensitivity test have levels higher than the 99th percentile, the sex-specific limit. Heart troponin levels were more significant in patients with preeclampsia or pregnancy-induced hypertension. In both pregnant and postpartum women, during pregnancy, cardiac troponin was a trustworthy independent predictor of hypertension or preeclampsia [15].

An early onset of cardiovascular disease is associated with preeclampsia. Preeclamptic women run the risk of ischemic heart disease and hypertension. To start preventative interventions, it's critical to identify women who are most at risk. We examined the relationship between the cardiac protein high-sensitivity troponin I (hs-cTnI) levels and hypertension and a history of preeclampsia with early onset in these at-risk mothers [16]. The sample of 339 women taken from Preeclampsia Risk Evaluation in Females, including 177 having a history of preeclampsia with early onset and 162 with a prior uncomplicated index pregnancy, had their hs-cTnI levels assessed 9–10 years after giving birth. Several statistical tests and linear regression analyses were used to analyze associations [17]. According to our research, women who had or did not have a history of early-onset preeclampsia did not vary from one another in their hs-cTnI levels. In contrast to their normotensive peers, present hypertensive women having a history of preeclampsia had hs-cTnI levels that were statistically substantially higher. Therefore, for women at risk for cardiovascular disease, hs-cTnI levels may aid in risk prediction [18].

A higher risk for cardiovascular disease earlier in life is linked to preeclampsia. Preeclamptic women run the risk of ischemic heart disease and hypertension. To start preventative interventions, it's critical to identify women who are most at risk [19]. We looked at the relationship between hypertension and a history of preeclampsia with early onset in these high-risk women and high-sensitivity cardiac troponin I (hs-cTnI) levels. 339 women from the Preeclampsia Risk Evaluation within FEMales sample, 177 of whom had a history with early-onset preeclampsia, & 162 with a prior uncomplicated index pregnancy, had their

hs-cTnI levels assessed 9–10 years after giving birth [20]. Some statistical tests and linear regression analysis were used to analyze associations. According to our research, women who had or didn't have a history of early-onset preeclampsia did not vary from one another in their hs-cTnI levels. In contrast to their normotensive peers, present Hs-cTnI levels in preeclampsia-affected hypertensive women were statistically substantially higher. Therefore, for women at risk for cardiovascular disease, hs-cTnI levels may aid in risk prediction [21].

Preeclampsia is a hypertension condition associated with pregnancy. Blood pressure issues have been linked to abnormal hormone levels. The study examined the correlation between worse PE-related sequelae, such as arterial hypertension, and postpartum mothers' blood levels like Progesterone, prolactin, estradiol, and ß-HCG. In the current study, 20 women with uncomplicated pregnancies and 30 preeclamptic patients each participated [22]. Following The blood ß-HCG, Progesterone, prolactin, and estradiol levels were assessed before and after delivery and on the initial and third postpartum days. Assessed with ECLIA. The postpartum mother's urine hormone levels & their relationship to preeclampsia blood pressure readings were discovered for the first time in this investigation [23]. In our opinion, preeclampsia's persistent arterial hypertension during pregnancy and the worsening of the disease's characteristics most likely lack any hormonal components. More extensive and focused prospective studies are advised. The goal of the study was to compare variations in “Mean platelet volume (MPV)," indicators for the Neutrophil-lymphocyte ratio/platelet-lymphocyte ratio, and patients with severe preeclampsia (PE) among typically pregnant and non-pregnant women are all examples of these ratios [24]. “Systemic Inflammatory Response (SIR)”. According to our research, there was no distinction in MPV levels between pregnant women in excellent health, those with severe PE, and women who are not pregnant. NLR cannot do the detection of patients having severe PE. PLR assessed before pregnancy termination is also a poor indicator of severe PE [25].

Conclusion

The study has concluded that the outcomes of this study indicate that markers such as the total leucocyte count, serum prolactin, and Troponin I can be considered as early predictors of peripartum cardiomyopathy (PPCM). Monitoring these markers can help identify those at risk and allow for appropriate treatments to prevent more issues from occurring. To keep a close eye on the progression of PPCM, it is advised to follow up with patients for five months carefully. In hypertensive pregnant individuals, early detection and intervention based on these indicators may lead to improved outcomes and the prevention of unfavorable cardiac events. It is important to remember that this study had a small sample size, which could have altered how widely applicable the results were. Brain natriuretic peptide evaluation as a PPCM marker was also impossible due to resource limitations and cost. In light of prolactin's probable function as a causal factor, future studies could look at the therapeutic potential of dopamine antagonists like Bromocriptine and cabergoline. More research is needed into the role of anti-inflammatory markers in PPCM diagnosis. More extensive studies can fill these knowledge gaps by providing more generalizable findings from a more comprehensive population sample.

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